REMARKS

Applicant respectfully requests entry of the Amendment and reconsideration of the claims.

Please cancel claims 20-31 without prejudice or disclaimer. Applicant reserves the right to pursue the subject matter of the cancelled claims in one or more continuation or divisional applications.

Applicant has amended claim 1 to clarify the claimed subject matter. Support for the amendment can be found throughout the specification, including lines 18-26 at page 5, lines 9-14 at page 16, line 26 at page 18 to line 2 at page 19, lines 11-16 at page 19, lines 12-24 at page 20, and Example 1 beginning at page 44. Claims 14-15, 17-18, and 32-33 have been amended to correct the claim limitation to match the antecedent basis of the claim depended upon.

Applicant has added new dependent claims 34-49. Support for the new claims can be found in the specification, for example at page 9, line 29 to page 10, line 3; page 11, line 30 to page 12, line 11; page 13, lines 23-28; page 37, line 8; and page 39, lines 3-9. No new matter has been added by the amendment or new claims.

Claims 1-11, 13-19, and 32-49 will be pending upon entry of this amendment. Claim 19 has been withdrawn from consideration by the Examiner.

Rejection for New Matter and Indefiniteness

Claims 1-11, 13-18, and 32-33 were rejected under 35 U.S.C. § 112, first and second paragraphs. The Examiner rejected the recitation "an effective amount of a combination..." as allegedly new matter under § 112, first and second paragraphs. In addition, the Examiner asserts the alleged new matter abrogates the benefit of priority to U.S. patent application USSN 60/280,805, filed April 2, 2001.

Without acquiescing to the rejection and solely for the purpose of expediting prosecution, Applicant has removed the objected to language from claim 1. Claim 1 as amended now recites an agent that arrests the growth of or causes deletion of cells expressing CD40 wherein the agent consists of a CD40 specific binding agent. Support for the amendment can be found in the specification, for example, at lines 18-26 on page 5, lines 9-14 on page 16, line 26 on page 18 to

line 2 on page 19, and lines 12-24 on page 20. The corresponding descriptions in U.S. provisional application 60/280,805 can be found at lines 5-14 on page 5, lines 3-8 on page 15, lines 16-26 on page 17, and line 32 on page 18 to line 6 on page 19.

"CD40 specific binding agent" and "CD20 specific binding agent" are described, for example, at lines 12-24 on page 20 and lines 3-27 on page 21. The corresponding descriptions in U.S. provisional application 60/280,805 can be found at line 32 on page 18 to line 6 on page 19 and line 20 on page 19 to line 6 on page 20. Support for a CD40 specific binding agent that stimulates CD40 can be found in the specification, for example, at lines 11-16 on page 19. The corresponding description in U.S. provisional application 60/280,805 can be found at line 35 at page 17 to line 2 on page 18.

Claim 1 as amended also recites that the combination of CD20 specific binding agent and CD40 specific binding agent inhibits the neoplastic disease or disorder. Support for the amendment can be found in the specification, for example, at working Example 1 and Figures 4 and 5. The corresponding descriptions in U.S. provisional application 60/280,805 can be found at Example 1 beginning at page 41 and Figures 4 and 5.

Applicant respectfully asserts the claims as amended are described and supported in both the instant application and in U.S. provisional application 60/280,805. In view of the foregoing, Applicant asserts that the amended claims do not contain new matter thereby providing a sufficient written description that is definite and should receive the benefit of priority of U.S. provisional application 60/280,805, filed April 2, 2001.

Withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 102(e)

Claims 1-11, 13-18, and 32-33 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. 2001/0018041 (hereinafter Hanna et al.). The Examiner also rejects claims 1-11, 13-18, and 32-33 under 35 U.S.C. § 103(a) as allegedly obvious over U.S. 2001/0018041 (Hanna et al.) in view of U.S. Patent No. 6,843,989 (Siegall et al.) and U.S. Patent No. 6,455,043 (Grillo-Lopez), and in further view of U.S. Patent No. 5,674,492 (Armitage et al.), Benoit et al. (1996), and U.S. 2005/0129689 (Fanslow et al.). Applicants respectfully traverse this rejection.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *See* MPEP 2131.01, citing *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). The identical invention must be shown in the same complete detail as is recited by the claims. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989).

Hanna et al. requires an anti-CD40L antibody, fragment thereof, or CD40L antagonist. See, for example, the Abstract and paragraph [0017]. A CD40L antagonist is defined in Hanna et al. as a molecule which interferes with the interaction of CD40L with its binding partner CD40. The stated purpose of inhibiting this interaction is interfering with CD40 signaling or blocking the signals of CD40, permitting the cell to survive and avoid IgM- or Fas- induced apoptosis. See Hanna et al. at paragraphs [0017], [0049], and [0117]. Therefore, a CD40 binding agent that stimulates CD40 is not a CD40L antagonist as defined in Hanna et al.

In stark contrast to Hanna et al., Applicant discloses administering a CD40 specific binding agent that stimulates CD40. See specification, for example, at page 19, lines 11-16. Applicant's claims as amended do not require a CD40L antagonist as defined in Hanna et al. and such a CD40L antagonist does not fall within the scope of the amended claims. Hanna et al. therefore does not disclose all the elements of the claims.

The Office Action alleges Hanna et al. discloses the particular combination of anti-CD20 antibodies and anti-CD40 antibodies at paragraph [0104] on page 10 of Hanna et al. The paragraph cited by the Examiner, however, also requires an anti-CD40L antibody or fragment thereof. See, for example, lines 1-5 of paragraph [0104]. As discussed above, Applicant's claims as amended do not require an anti-CD40L antibody and an anti-CD40L antibody does not fall within the scope of the amended claims.

In view of the forgoing, Applicant submits Hanna et al. does not anticipate the claims. The reference does not disclose all the elements of the claims as amended. Withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

Claims 1-11, 13-18, and 32-33 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over Hanna et al. in view of U.S. Patent No. 6,843,989 (hereinafter Siegall et al.) and

U.S. Patent No. 6,455,043 (hereinafter Grillo-Lopez), and in further view of U.S. Patent No. 5,674,492 (hereinafter Armitage et al.), Benoit et al. (1996), and U.S. 2005/0129689 (hereinafter Fanslow et al.). Applicants respectfully traverse this rejection.

To make a *prima facie* case of obviousness, the teachings of the prior art should have suggested the claimed subject matter to the person of ordinary skill in the art, and all the claim limitations must be taught or suggested in the references cited by the Examiner. *In re Kotzab*, 217 F.3d 1365, 1370 (Fed. Cir. 2000). As articulated by the Supreme Court in a recent case, a combination is obvious if it is no more than the predictable use of known elements according to their established functions and there was a reason to combine the known elements. *KSR Int'l Co. v. Teleflex, Inc.*, 127 S.Ct. 1727 (2007). To make a *prima facie* case of obviousness, "it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed." *Id.* A "reasonable expectation of success" is the standard with which obviousness is determined. MPEP § 2141; *Hodosh v. Block Drug Co.*, 786 F.2d 182, 187 n.5 (Fed. Cir. 1986).

The initial burden to make a *prima facie* case of obviousness is on the Examiner. *In re Bell*, 991 F.2d 781, 783 (Fed. Cir. 1993). The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also contains a motivation or suggestion to modify or combine the references. *In re Mills*, 916 F.2d 680, 682 (Fed. Cir. 1990). "A rejection cannot be predicated on the mere identification . . . of individual components of the claimed invention." Rather, particular findings must be made as to the reason the skilled artisan, with no known knowledge of the claimed invention, would have selected these components for combination in the manner claimed." *Ecolochem Inc. v. Southern Calif. Edison Co.*, 227 F.3d 1361, 1375 (Fed. Cir. 2000).

Applicants submit the Office Action has not established a *prima facie* case of obviousness because Hanna et al. teaches away from Applicant's claims. As discussed above, Hanna et al. requires an anti-CD40L antibody, fragment thereof, or CD40L antagonist. The stated purpose in Hanna et al. for inhibiting the interaction of CD40L with its binding partner CD40 is interfering with CD40 signaling or blocking the signals of CD40 permitting the cell to survive and avoid IgM- or Fas- induced apoptosis. See Hanna et al. at paragraphs [0017], [0049], and [0117]. A CD40 binding agent that stimulates CD40 is therefore not a CD40L

antagonist as defined in Hanna et al. By requiring an anti-CD40L antibody or other CD40L antagonist, Hanna et al. specifically teaches away from administering an agent that arrests the growth of or causes deletion of cells expressing CD40, wherein the agent consists of a CD40 specific binding agent that stimulates CD40. Applicant's claims as amended do not require a CD40L antagonist as defined in Hanna et al. and such a CD40L antagonist does not fall within the scope of the amended claims.

If a proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. MPEP § 2144(VI); *In re Ratti*, 270 F.2d 810 (CCPA 1959). As discussed above, Hanna et al. clearly requires a CD40L antagonist. Removing the CD40L antagonist from the combination disclosed by Hanna et al. would therefore change the principle of operation of the prior art method being modified.

None of the secondary references cure the deficiencies of Hanna et al. Siegall et al. and Fanslow et al. only disclose anti-CD40 antibodies and do not teach or suggest combining anti-CD40 antibodies with anti-CD20 antibodies. Grillo-Lopez only discloses anti-CD20 antibodies and does not teach or suggest combining anti-CD20 antibodies with anti-CD40 antibodies. Both Armitage et al. and Benoit et al. disclose anti-CD20 antibodies and anti-CD40 antibodies. However, Armitage et al. does not teach or suggest combining anti-CD20 antibodies and anti-CD40 antibodies, and Benoit et al. requires a crosslinking agent or GAM that crosslinks the anti-CD20 and anti-CD40 antibodies. Absent Applicant's disclosure, none of the secondary references provide any motivation for excluding the CD40L antagonist required by Hanna et al.

In contrast to Benoit et al., Applicant's claims as amended are clearly directed to a CD40 specific binding agent and CD20 specific binding agent wherein the combination inhibits the neoplastic disease or disorder. The claimed combination does not encompass a crosslinking agent. Working example 1 shows that the combination of anti-CD20 and anti-40 antibodies is sufficient to inhibit the neoplastic cells *in vivo*. See specification, for example, at pages 44-46. These results were unexpected and surprising in view of Benoit et al., which required a crosslinking agent for therapeutic activity.

In view of the forgoing, Applicant submits the Office Action has failed to establish a *prima facie* case of obviousness. The cited combination of references fails, in the least, to

provide a motivation for modifying Hanna et al. to arrive at Applicant's. Moreover, the primary reference Hanna et al. teaches away from the claims as amended. Absent Applicant's disclosure, none of the secondary references provide any motivation for excluding the CD40L antagonist required by Hanna et al. Withdrawal of the rejection is respectfully requested.

Summary

In view of the above amendments and remarks, Applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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